CHAPTER 14

H.P. 432 - L.D. 599

Resolve, Directing a Review of the Effects of Antifreeze, Engine Coolant and Aversive Agents on the Environment and Small Animals

Sec. 1. Review. Resolved: That the Department of Environmental Protection in cooperation with the Department of Health and Human Services, Bureau of Health and the Department of Agriculture, Food and Rural Resources shall review the effects of antifreeze, engine coolant and aversive agents, including denatonium benzoate, on the environment and small animals. The Department of Environmental Protection shall report its findings to the Joint Standing Committee on Natural Resources by January 30, 2006. The Joint Standing Committee on Natural Resources is authorized to report out legislation in connection with the review to the Second Regular Session of the 122nd Legislature.

Scope:

This report attempts to answer questions regarding effects of antifreeze and denatonium benzoate on the environment and small animals. In addition human toxicology, efficacy, cost and current use of denatonium benzoate will be reviewed. For this report the department solicited input and comment from the Bureau of Remediation and Waste Management (BRWM) staff chemist, senior hydrogeologist as well as the State Toxicologist and Veterinarian. No actual studies or experiments were carried out, and all information was obtained from published studies, published reports, and telephone calls to knowledgeable parties.

General Information:

There are two types of antifreeze in general use, ethylene glycol and propylene glycol. According to the Agency for Toxic Substances and Disease Registry(ATSDR):[1] "Both ethylene glycol and propylene glycol are clear, colorless, slightly syrupy liquids at room temperature. Either compound may exist in air in the vapor form, although propylene glycol must be heated or briskly shaken to produce a vapor. Ethylene glycol is odorless but has a sweet taste. Propylene glycol is practically odorless and tasteless."

Both of these liquids are very soluble in water, are highly mobile when released to soil and biodegrade relatively quickly in the environment. Ethylene glycol is very toxic to humans and other animals when ingested. Propylene glycol has a much lower toxicity but is slightly more expensive than ethylene glycol.

The ASTDR further states, “The Food and Drug Administration (FDA) has classified propylene glycol as an additive that is ‘generally recognized as safe’ for use in food. It is used to absorb extra water and maintain moisture in certain medicines, cosmetics, or food products. It is a solvent for food colors and flavors.”[2]

A small amount of denatonium benzoate can make ethylene glycol unpalatable to most people and many animals. However, there are some unanswered questions about the toxicity, efficacy, and environmental fate of this additive.

Use:

The states of California and Oregon currently have laws requiring a bittering agent be added to ethylene glycol antifreeze. Additionally, S.1110 and H.R.2567 (federal bills requiring a bittering agent) are currently being considered in the U.S. Congress.

Oregon has required bittering agent be applied to ethylene glycol antifreeze and windshield washing fluid that contains methanol in concentrations of 4% or greater since the beginning of 1994. The bittering agent used is denatonium benzoate, and the required minimum concentration is 30 ppm for both the ethylene glycol antifreeze and the windshield washer fluid. The levels placed in the antifreeze and windshield washing fluid typically range between 30 ppm and 50 ppm.

In 1960 denatonium benzoate was approved for use in the United States for toiletries, cosmetics and industrial uses. It is currently used in a variety of products, including: denatured alcohol, deer repellant, nail biting aversive, windshield washing fluid and coatings for electrical cables to discourage rodent damage.

Toxicology:

Ethylene glycol is a toxic chemical that humans and animals are frequently exposed to as antifreeze. The sweet taste and colorful presentation of the product have led to occasional accidental exposures of children and pets. Two options for dealing with this problem have been presented. The first is to add a bittering agent, denatonium benzoate, to antifreeze. The second is to replace ethylene glycol antifreeze with propylene glycol antifreeze.

Ethylene glycol. The toxicity of ethylene glycol has been reasonably well established through case reports of accidental exposure leading to death and through more systematic assessments in animals. The toxicity of ethylene glycol in humans largely derives from its metabolism to glycolic acid.

Ingestion of a high or lethal dose generally results in central nervous system depression within 2 hours and cardiopulmonary toxicity within 24 hours. Acute renal toxicity, due to metabolic acidosis and the deposition of insoluble calcium oxalate crystals in the kidney, becomes apparent within 72 hours. Neurological effects may appear several days after ingestion as a result of cranial nerve damage.

EPA lists a reference dose (RfD) of 2 mg/kg-d for oral exposure to ethylene glycol based on observations of kidney toxicity in chronically exposed rats. This RfD is thought to be protective of developmental and reproductive effects that have also been observed in rats and mice. The entry for ethylene glycol on EPA's database for risk assessment - Integrated Risk Information System (IRIS) - does not contain any information on noncancer inhalation risks or cancer risks by any route of exposure.

LD stands for "Lethal Dose". LD50 is the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals. The LD50 is one way to measure the short-term poisoning potential (acute toxicity) of a material. LD_{50}s for ethylene glycol range from 5.5-13 mL/kg in rodents. Humans appear to be more sensitive, with an estimated lethal dose of 1.4 mL/kg[3] or 1.6 g/kg[4]. Cats may be roughly as sensitive as humans; a 1961 report suggested that the minimal lethal dose for cats is 1 g/kg[5].

Propylene glycol. Propylene glycol is practically odorless and tasteless[6]. The toxicity of propylene glycol is not as well understood as that of ethylene glycol, although it is generally agreed that propylene glycol is much less toxic. The metabolites of propylene glycol, unlike the toxic metabolites of ethylene glycol, are normal constituents of carbohydrate metabolism. The Food and Drug Administration considers propylene glycol to be "generally recognized as safe" and it is used as a food and pharmaceutical additive. It has also been suggested as an effective antidote for ethylene glycol poisoning[7].

EPA's IRIS does not list any toxicity information for propylene glycol. The last revision of this listing was made in 1991, at which time EPA concluded that there were insufficient data for deriving an inhalation risk value. New information was identified by EPA in 2002 but this is still being reviewed internally. No information is given for oral noncancer risks or cancer risks.

LD_{50}s are reported to be 18-30 g/kg in rats, rabbits and dogs[8]. This suggests, very roughly, that the acute toxicity of propylene glycol is 10-20 times less than that of ethylene glycol.

Denatonium benzoate. Little is known about the toxicity of denatonium benzoate. One report from the California EPA, intended to discuss the toxicity of denatonium saccharide, includes references to several studies of denatonium benzoate that are generally judged to be unreliable[9]. These include:

1) A two-year study of rats in which no effects were noted at average doses up to 16 mg/kg-d. CalEPA judged the study “not acceptable” due to multiple deficiencies in design and conduct.
2) A one-year study of monkeys in which there were observations of deaths that were possibly treatment-related, but without clinical signs of organ toxicity, at 8 or 16 mg/kg-d. The No Observed Effect Level in this study was 1.6 mg/kg-d. This study was also judged unacceptable due to “major deficiencies”.
3) An acute toxicity study in rats and rabbits administered single gavage doses of denatonium benzoate. LD_{50}s of 640 (male) and 584 (female) mg/kg were estimated in rats and LD_{50}s of 508 (male) and 640 (female) mg/kg were estimated in rabbits. This study reported symptoms in rats including diarrhea and decreased activity at dose levels of 127-320 mg/kg and salivation, ataxia, tremors, and decreased respiratory rate at higher doses.
4) A companion assessment to the acute toxicity study in which acute toxicity in neonatal rats was observed at much lower doses (LD_{50} 23 mg/kg). This assessment was judged to be unacceptable due to design flaws.

These data, to the extent that they can be trusted, suggest that denatonium benzoate may have an acute toxicity as high or higher than that of ethylene glycol, although the dilution of the agent would have to be considered in assessing its impact on the toxicity of an antifreeze mixture.

Value for small animals:

Antifreeze (ethylene glycol) is well known to be an extremely hazardous substance if ingested by dogs and cats. If veterinary treatment is not begun within a few hours of exposure, one teaspoonful of ethylene glycol can be fatal to a 10-pound cat, while one to two tablespoonfuls can kill a 100-pound dog. A less toxic form of antifreeze, propylene glycol, is safer than ethylene glycol, but can still cause poisoning if consumed in large enough quantities. The problem of antifreeze toxicity is exacerbated by the fact that animals may be attracted to it, and pets-especially dogs-continue to be exposed and die each year. The American Veterinary Medical Association has taken a position of "support" on the legislation currently in the United States Congress, H.R. 2567/S. 1110, the Engine Coolant and Antifreeze Bittering Act of 2005.

The Maine Veterinary Medical Association placed this subject before its members at their Annual Meeting on January 7, 2006, and subsequentially provided (via email) all members with detailed information on the subject, including the preliminary DEP risk-benefit assessment. The near-unanimous response from the membership is that Maine’s veterinarians continue to see cases of ethylene glycol poisoning in their practices each year (perhaps an average 2-3 cases per practice). The incidence is less than it once was, perhaps

because of increased use of propylene glycol. However, the toxic risk to small animals from antifreeze remains significant, and the addition of a bittering agent would be very welcome, provided such agent does not pose environmental risks on the scale of MTBE.

Efficacy:

Efficacy refers to evidence that denatonium benzoate is effective in preventing ingestion of ethylene glycol. While there is clearly evidence that denatonium benzoate is a bitter tasting substance, it is a separate question as to whether it can prevent accidental ingestion of toxic amounts of antifreeze.

We are aware of one study testing the efficacy of using denatonium benzoate. Mullins and Horowitz[10] assessed ethylene glycol poisoning among Oregon children (<6 years old) before and after the use of denatonium benzoate was mandated by state law. The mean number of annual pediatric poisonings to ethylene glycol was 17.8 from 1987 through 1994. In 1995 the law requiring addition of denatonium benzoate was implemented. From 1996 through 2003 the mean number of annual poisonings was 20.6. None of the 332 exposures in the 16-year period resulted in major effects or death. The authors concluded that the rate of pediatric ethylene glycol poisonings was not significantly different after the implementation of the denatonium benzoate rule.

The US Consumer Product Safety Commission (CPSC) published a report on aversive agents in 1992. This study focused mainly on denatonium benzoate, as it was the agent for which the majority of information was submitted[11]. This report reviewed the available information on the effectiveness of denatonium benzoate in preventing ingestion of a toxic liquid; it was determined that aversive agents are unlikely to prevent ingestion of one or two “swallows” of a liquid. One or two swallows could represent a toxic or lethal dose of ethylene glycol for a small child. CPSC concluded that “the use of aversive agents should not be considered for regulation until the effectiveness of these substances to limit ingestion is demonstrated”.

CPSC noted that virtually all toxicity information available for denatonium benzoate is acute exposure information, with a lack of carcinogenicity or teratogenicity data and very limited chronic exposure information. Although CPSC concluded that the use of denatonium benzoate as an aversive agent would not result in acute toxicity, it also commented that the environmental impact of this compound, which is not thought to biodegrade entirely, is unknown.

These reports do not provide evidence that denatonium benzoate has an effect on ethylene glycol exposures, fatal or otherwise. The report of Mullins and Horowitz (2004) suggests that most pediatric exposures to ethylene glycol are not lethal and therefore likely represent small volumes of ingestion (1 “swallow” or less). Both reports suggest that denatonium benzoate would not deter a child from ingesting this volume.

Environmental Fate:

Ethylene Glycol:[12] Ethylene glycol's production and uses such as a coolant and antifreeze ”may result in its release to the environment through various waste streams”. If released to air, a vapor pressure of 0.092 mm Hg at 25 deg C indicates ethylene glycol will exist solely as a vapor in the ambient atmosphere. Vapor-phase ethylene glycol will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 2 days. Ethylene glycol is not expected to be susceptible to direct photolysis by sunlight since it does not contain functional groups that are expected to absorb light with wavelengths >290 nm.

If released to soil, ethylene glycol is expected to have very high mobility based upon an estimated partitioning coefficient [Koc, or how well a substance will bind to organic carbon in the soil] of 1. Volatilization from moist soil surfaces is not expected to be an important fate process based upon a Henry's Law constant of 6.00X10-8 atm-cu m/mole. [The Henry’s Law constant is a measure of how well a substance will enter the air, once dissolved in water. The higher the number, the more that will enter the air.] Ethylene glycol is not expected to volatilize from dry soil surfaces based upon its vapor pressure. Ethylene glycol is biodegraded in soil 97-100% in 2-12 days.

If released into water, ethylene glycol is not expected to adsorb to suspended solids and sediment based upon the estimated partitioning coefficient. In a river die-away test, degradation was complete within 3 days at 20 deg C and 5-14 days at 8 deg C. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's Henry's Law constant. A bioconcentration factor (BCF) of 10, reported for ethylene glycol in fish, Golden ide (Leuciscus idus melanotus), after 3 days of exposure suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions.

Propylene Glycol:[13] Propylene glycol's production and use as an emollient in cosmetics and pharmaceutical creams, a corrosion inhibitor, the manufacture of resins, an additive to paint to provide freeze-thaw stability, solvent in food colors and flavors and as an airplane de-icing fluid may result in its release to the environment through various waste streams.

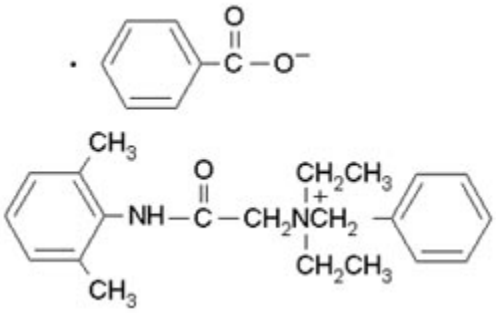
If released to air, a vapor pressure of 0.13 mm Hg at 25 deg C indicates propylene glycol will exist solely as a vapor in the ambient atmosphere. Vapor-phase propylene glycol will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 32 hours.

If released to soil, propylene glycol is expected to have very high mobility based upon an estimated partitioning coefficient [Koc] of 8. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of 1.3X10-8 atm-cu m/mole. Propylene glycol is not expected to volatilize from dry soil surfaces based upon its vapor pressure. Propylene glycol was mineralized 73-78% in laboratory studies conducted using an agricultural soil over a 51 day incubation period, suggesting biodegradation will be an important environmental fate process in soils.

If released into water, propylene glycol is not expected to adsorb to suspended solids and sediment based upon the estimated partitioning coefficient [Koc]. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. Numerous screening studies using wastewater or sewage inoculum as seed, suggests that propylene glycol will be degraded readily in aqueous environments. Propylene glycol is not expected to undergo hydrolysis since this compound lacks functional groups that hydrolyze under environmental conditions. An estimated bioconcentration factor [BCF] of 3 suggests the potential for bioconcentration in aquatic organisms is low.

Occupational exposure to propylene glycol may occur through inhalation and dermal contact with this compound at workplaces where propylene glycol is produced or used. Propylene glycol is contained in a number of consumer products including cosmetics, pharmaceutical creams and some food additives. The general population may be exposed to propylene glycol through dermal and ingestion pathways when products containing this compound are used. Propylene glycol is also used in aerosol mists that are commonly employed in hospitals and public buildings for disinfection purposes; therefore, the general population may be exposed to this compound by inhalation routes.

Denatonium benzoate:
Denatonium benzoate is a white powder with this chemical structure:



Denatonium benzoate is a solid at normal temperatures, with a melting point of 166-170^{o}C. It would not be expected to volatilize to air. The partitioning coefficient [K_{oc}] of denatonium benzoate has been determined in one study to be 0.9 and the solubility in water is 45 g/L at 20^{o}C. From these data it is expected that denatonium benzoate released to soil will be highly mobile. It will readily dissolve in water and not be bound to soil particles. The denatonium ion may persist in ground water.

According to the *Material Safety Data Sheet* for a commercial formulation called **AVERSION®,** denatonium benzoate is biodegradable and not known to bioaccumulate. The manufacturers of another commercial formulation called **Bitrex** report a biodegradation half life, derived under laboratory conditions and temperature of about 20^{o}C, of approximately 45 days[14]. However, in a study by the Society of Automotive Engineers[15], the denatonium ion does not biodegrade during treatment in a typical waste water treatment plant. The paper suggests that degradation of benzoate is primarily responsible for the reported biodegradation, and that the denatonium ion, responsible for the aversive taste of the compound, is not easily biodegradable. No other information was located on biodegradability.

Ken Kauffman, a toxicologist with the State of Oregon, stated in a telephone conversation with DEP staff that no incidents of drinking water well contamination or groundwater contamination or bad tasting water due to denatonium benzoate have become known. The one known case of drinking water well contaminated with antifreeze was a case of sabotage. Someone deliberately poured a gallon of antifreeze directly into a well. The well was purified by heavy and repeated pumping to remove the antifreeze. Denatonium benzoate was never detected, but it was never tested for either. The contaminant tested for was glycol. When the glycol concentration was below a certain minimum level (possibly the level of “not detected”) the well was considered clean. See the section “A Sense of Scale” below.

Cost Comparisons : Phone calls to various stores by DEP staff showed that the less toxic, polypropylene glycol antifreeze costs approximately $2 per gallon more than the standard ethylene glycol antifreeze.

Ken Kauffman, a state toxicologist for the state of Oregon told DEP staff that Oregon has been informed adding the bittering agent to antifreeze increases the retail cost of antifreeze from 1 - 4 cents per gallon.

The manufacturer of Prestone antifreeze states that adding bittering agent to antifreeze will increase the cost by only a couple of pennies per gallon at the manufacturing level. A representative of Corporate Relations for Honeywell, the company that owns Prestone, stated in a phone call with DEP staff that the cost of the bittering agent is not the significant issue that Honeywell is worried about. Rather it is the much more significant impact to the distribution network and the need to retool existing facilities to manage different formulations of product to address a requirement for a single state.

Honeywell states California, Oregon, and New Mexico require the addition of a bittering agent in ethylene glycol based antifreeze products and are within the same distribution network. All three states address the issue of liability associated with the bittering agent by specifically assigning liability for any damage resulting from the bittering additive to the manufacturers of the bitterant. It is possible that other states besides California, Oregon, and New Mexico are receiving ethylene glycol with bittering agent added even though it is not required in those states.

Honeywell states that accommodating the requirement of a single state in the eastern region of the nation to add bittering agent will cause logistical problems with the distribution network. Namely, extra effort will be required to supply one state, such as Maine, with ethylene glycol antifreeze containing a bittering agent, while at the same time supplying the other states supplied by the same factory with standard ethylene glycol antifreeze (antifreeze without the bittering agent). Therefore, in the eastern region, the costs associated with the requirement to add the bittering agent could be much more significant than simply the cost of the raw materials.

A Sense of Scale:

Will denatonium benzoate be the next MTBE? The concentrations of denatonium benzoate released to the environment will likely be much smaller than concentrations of MTBE that were released in gasoline spills. However the only way to be certain that denatonium benzoate will not impact wells from antifreeze spills is to do a fate and transport study using a controlled release in an experimental aquifer like the University of Waterloo, Canada did for gasoline constituents and chlorinated solvents in the Borden aquifer.

To theoretically compare the potential release of denatonium benzoate to the environment from automotive engine coolant with the release of methyl *tert*-butyl ether [MTBE] from gasoline consider the following:

- A car with average fuel economy [30 miles/ gallon] and average annual mileage [12,000 miles] consumes 400 gallons of gasoline per year. If the gasoline is a reformulated mixture it would contain an average of 11% MTBE, for a total of 44 gallons or 123,000 grams of pure MTBE. If the gasoline was a typical non-reformulated mixture containing only 2% MTBE, only 8 gallons or 22,400 grams would be consumed.

  The same car would likely use less that 2 gallons of engine coolant. The amount of denatonium benzoate contained in those 2 gallons would be 0.228 grams if the coolant contained the recommended 30 mg/L concentration. (1 mg/L = 1 ppm.)

- One gallon of reformulated gasoline, if spilled, would release a mass of 308g of MTBE to the environment. It would take 2704 gallons of treated antifreeze to release an equivalent mass of denatonium benzoate.

End Notes:

[1] ATSDR ToxFAQs™ for Ethylene Glycol and Propylene Glycol, September 1997 http://www.atsdr.cdc.gov/tfacts96.html

[2] ibid

[3] Klaassen CD, ed. 1996. Casarett and Doull's Toxicology, fifth edition. McGraw-Hill.

[4] Hess R et al. 2004. Ethylene glycol: an estimate of tolerable levels of exposure based on a review of animal and human data. Arch Toxicol 78:871-80.

[5] Klaassen CD, ed. 1996. Casarett and Doull's Toxicology, fifth edition. McGraw-Hill.

[6] Agency for Toxic Substances and Disease Registry (ATSDR). 1997. Toxicological Profile for ethylene glycol and propylene glycol. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

[7] Klaassen CD, ed. 1996. Casarett and Doull's Toxicology, fifth edition. McGraw-Hill.

[8] ibid

[9] CalEPA 2000. Summary of toxicology data: Denatonium saccharide. California Environmental Protection Agency, Department of Pesticide Regulation, Medical Toxicology Branch. T20000330.doc/March 30 2000. www.cdpr.ca.gov/docs/toxsums/pdfs/3981.pdf

[10] Mullins ME and Horowitz BZ 2004. Was it necessary to add Bitrex (denatonium benzoate) to automotive products? Vet Human Toxicol 46(3):150-4.

[11] US Consumer Product Safety Commission (CPSC) 1992. Final report: Study of aversive agents.

[12] Center for Disease Control Hazardous Substance Database **http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~N3bLf8:1**

[13] Center for Disease Control Hazardous Substance Database **http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~N3bLf8:1**

[14] Evaluation Of The Fate And Transport Of Methanol In The Environment: **http://www.methanol.org/pdf/evaluation.pdf**

[15] Corby, JE and Doi, J et al. March 1-5, 1993, Biodegradability of a Denatoniun Bitterant, SAE Technical Paper Series 930587 (SAE International: The Society of Automotive Engineers, International Congress and Exposition, Detroit, MI, March 1993)